Linguistic and extralinguistic abilities in dementia

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Abstract

Progressive and relatively circumscribed loss of semantic knowledge, referred to as semantic dementia (SD) which falls under the broader umbrella of frontotemporal dementia, was officially identified as a clinical syndrome less than 50 years ago. Here, we review recent neuroimaging, pathological, and genetic research in SD. From a neuroimaging perspective, SD is characterised by hallmark asymmetrical atrophy of the anterior temporal pole and anterior fusiform gyrus, which is usually left lateralised. Functional magnetic resonance imaging (fMRI) studies have revealed widespread changes in connectivity, implicating the anterior temporal regions in semantic deficits in SD. Task-related fMRI have also demonstrated the relative preservation of frontal and parietal regions alongside preserved memory performance.

Keywords: Semantic-variant primary progressive aphasia, Frontotemporal dementia, Primary progressive aphasia

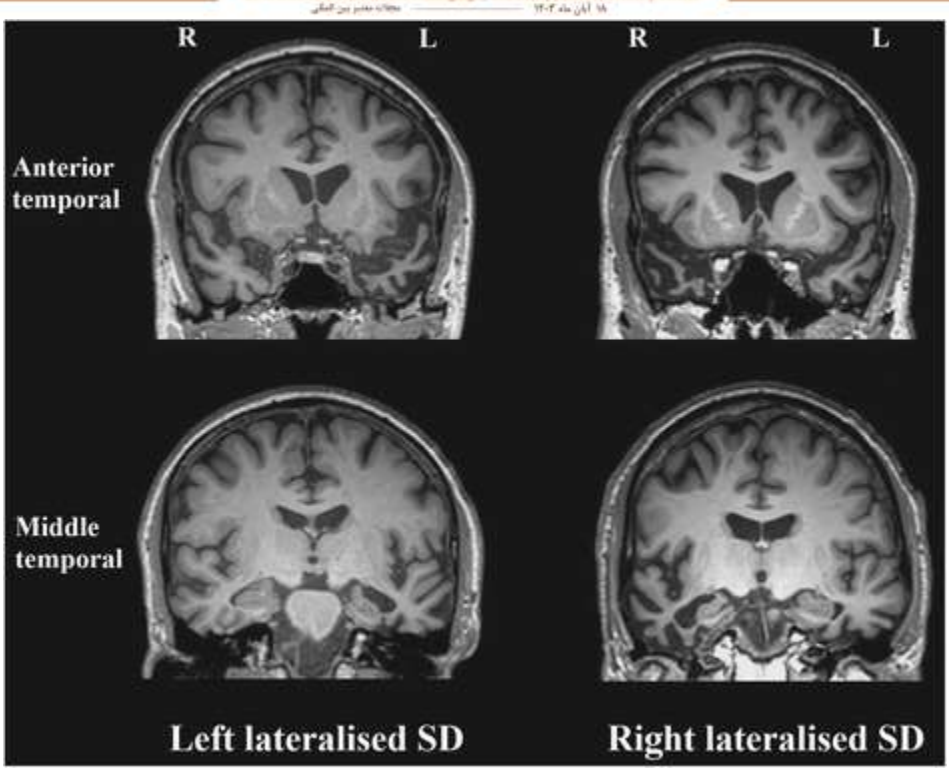
Introduction

A fascinating aspect of human cognition is the innate capacity to infer the thoughts, feelings, beliefs and intentions of others, known as theory of mind (ToM). Our unique aptitude to spontaneously consider perspectives distinct from our own is fundamental to successful social interactions, enabling us to describe, explain and predict behaviour based on the mental states of others [1]. Semantic dementia (SD), a progressive neurodegenerative disorder affecting language, was empirically described only relatively recently. In the early 1970s, the conceptualisation of memory into two distinct systems, an episodic system and a semantic system by Tulving [1], coincided with the report by Warrington [2] of three individuals who presented with visual object agnosia, a profound inability to recognise or identify objects. In light of this new memory system and additional assessment, Warrington recognised that the constellation of symptoms of these patients could be conceptualised as an underlying loss of semantic memory. Since this seminal paper, the syndrome, which is characterised by circumscribed but profound loss of semantic knowledge, has been referred to as SD [4] and, more recently, as semantic-variant primary progressive aphasia (PPA) [5]. Less than 50 years later, our understanding of this striking clinical syndrome has advanced. In this review, we will consider how recent studies in imaging, genetics, and pathology over the last decade have informed our knowledge of SD. Contemporary consensus criteria for SD require individuals to first meet criteria for PPA; i.e. the most prominent clinical symptom to be in the domain of language, and evidence of subsequent impaired activities of daily living. Then, sub-classification as semantic-variant is based on impaired confrontation naming *and* single-word comprehension, with supportive features including impaired object knowledge, surface dyslexia or dysgraphia, spared repetition, and spared speech production. In a series of 100 cases all of whom underwent longitudinal follow-up, the mean age at presentation was 64.2 years but with a range of 40–79 years [6]. There was a 50% survival of 12.8 years indicating a slower progression than in other forms of frontotemporal dementia [6]. Studies of the prevalence and incidence of SD have been relatively limited; however, a recent epidemiology study estimated the prevalence of frontotemporal dementia at 10.8/100,000, with SD accounting for approximately one-third of these cases [7] in line with previous estimates [8]. Whether this prevalence is similar across countries, however, remains to be examined, as most existing epidemiological data hail from European studies.

Clinically, patients with SD show a speech profile that is relatively fluent but empty of content, producing a pattern of so-called logorrhoea. Importantly, loss of semantic knowledge is observed irrespective of testing modality [9]. Impaired word comprehension is a mandatory feature and patients demonstrate word alienation in that they are able to repeat words such as “violin” or “caterpillar” but have no idea of their meaning. This deficit gradually progresses from low frequency and less familiar words, such as those mentioned, to more common words. Adlam et al. [10] demonstrated that SD patients are also impaired on non-verbal semantic matching tasks, tests of colour knowledge, sound knowledge, and object-use knowledge, which do not require naming or verbal comprehension even from an early stage of the disease. Such findings have provided evidence that, in SD, symptomatology reflects a profound and progressive loss of conceptual knowledge which is not limited to performance on verbal tasks [11]. There is also accompanying surface dyslexia: patients are unable to correctly pronounce irregular words such as pint which they read to rhyme with hint or flint.In contrast, recent studies have confirmed that episodic memory is relatively preserved in SD, particularly when tasks with minimal conceptual loading

are employed [1]. The intact performance on traditional non-conceptually loaded episodic memory tasks converges with the performance of SD patients on autobiographical memory tasks. Patients typically show relatively preserved recollection of recent autobiographical memory in the context of poorer remote autobiographical memory (known as the reverse temporal gradient or step-function), reflecting increased semanticisation of past events (e.g. [3]). This is in stark contrast to the compromised ability of SD patients to project forwards in time to imagine possible future events (e.g. [3]). These deficits in future-oriented thought are attributable to semantic processing impairments, and have led to the advancement of the *semantic scaffolding hypothesis* which proposes that semantic knowledge is required to impart structure and meaning during the process of future simulation [4].

Changes in behaviour and social cognition are increasingly recognised in SD [5]. Clinically, SD patients often show mental rigidity and inflexible behaviour. For example, patients may become obsessive in tasks they engage in (e.g. we have noticed patients spending hours completing jigsaw puzzles), food preferences (usually restricted to specific foods), or daily routines (e.g. clockwatching). In addition, SD patients may have increased apathy and changes in eating behaviour, as well as loss of empathy, impaired emotion perception and emotional memories, and reduced theory of mind capacity [4]. Over time, many patients become essentially mute with only a limited repertoire of stereotypic phrases and a complete loss of word comprehension. An extensive body of brain imaging studies have investigated structural and functional brain abnormalities in patients with SD. At presentation, visual inspection of magnetic resonance imaging (MRI) typically reveals hallmark bilateral, but asymmetric atrophy of the anterior temporal lobes, which is usually left lateralised . With the development of neuroimaging techniques to statistically measure this degeneration, whole-brain structural MRI studies using voxel-based morphometry (VBM) have confirmed grey matter loss, which is relatively localised to the temporal lobe (left-predominant), with some involvement of frontal and limbic regions (e.g. [6]). Specifically, these regions include asymmetric but bilateral involvement of the temporal pole, the fusiform gyrus, middle and inferior temporal gyrus, ventromedial prefrontal cortex, amygdala, hippocampus, and the insula, which have been confirmed by a recent meta-analysis [6]. Importantly, the asymmetric hippocampal involvement is also considered one of the hallmark features of SD. In addition, surface-based imaging studies have demonstrated predominantly left anterior temporal cortical thinning on both the lateral and ventral surfaces of the temporal lobe (e.g. [7]). Debate continues concerning the most critical region, but it appears that bilateral atrophy of the anterior fusiform region is required to generate the syndrome of SD.



More recently, white matter changes in SD have also been mapped using diffusion tensor imaging (DTI) and tractrography analyses. These studies have demonstrated that patients with SD also have reduced white matter integrity in the left temporal lobe, periventricular white matter, corpus callosum, and in white matter tract areas of the fornix, inferior longitudinal fasciculus, and the uncinate fasciculus [3]. Studies using DTI have also shown reduced structural connectivity in frontotemporal pathways in SD, particularly in the uncinate, arcuate, and inferior longitudinal fasciculi [3]. Although a range of DTI metrics have been applied across studies, the areas of abnormality show spatial overlap and are mostly adjacent to regions showing grey matter atrophy [4]. Recently, a tractrography study has uncovered the role of the frontal aslant tract in verbal fluency whilst degeneration of the uncinate fasciculus is uniquely correlated with semantic deficits. A proportion of patients present with right greater than left lateralised atrophy, referred to as right SD, or right temporal variant frontotemporal dementia [5]. These patients often present with profound behavioural changes, which can make distinction from the behavioural variant of frontotemporal dementia challenging [5]. Importantly, increasing evidence has revealed that the extent of behavioural and social cognition changes is related to integrity of the right temporal pole in this syndrome [2]. Patients with right lateralised atrophy also tend to show greater social cognition deficits than patients with left lateralised SD, while a subset present with prosopagnosia as the primary clinical feature [2]. Improved diagnosis of right SD, together with better understanding of features which give rise to the manifestation of this syndrome, will be important for future studies to address.

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In this part, we review recent evidence for the relationship between extralinguistic cognitive and language abilities in dementia. A survey of data from investigations of three dementia syndromes (Alzheimer's disease, semantic dementia and progressive nonfluent aphasia) reveals that, more often than not, deterioration of conceptual organization appears associated with lexical impairments, whereas impairments in executive function are associated with sentence- and discourse-level deficits. These connections between extralinguistic functions and language ability also emerge from the literature on cognitive reserve and bilingualism that investigates factors that delay the onset and possibly the progression of neuropsychological manifestation of dementia. Language deficits are frequent in dementia: Patients with dementia demonstrate, among other signs, word-finding problems (anomia), sentence comprehension deficits, and lack of cohesion in discourse. Unlike aphasias that are due to focal brain damage, language deficits in dementia occur in the context of multiple cognitive impairments. We first review relevant data from three dementia syndromes: dementia of the Alzheimer's type (DAT) and two variants of frontotemporal dementia (FTD): semantic dementia (SD) and primary progressive nonfluent aphasia (PNFA). These 2 KEMPLER AND GORAL three syndromes can be distinguished by their impairment patterns and distribution of neuropathology. DAT is characterized by a progressive deterioration of memory and at least two other cognitive domains (such as language, visuospatial perception, executive function). The neuropathology of Alzheimer's disease involves regions throughout the brain, particularly the hippocampus and areas in the frontal cortex [8]. Two varieties of FTD are distinguished from other dementia syndromes by their marked language impairments.[1] One FTD variant, SD, is characterized by fluent speech output accompanied by anomia and comprehension impairments. The neuropathology of SD appears to be primarily temporal in distribution. SD can be clinically confused with DAT in those patients with DAT who show relatively early and circumscribed language impairment. Another FTD variant, PNFA, is characterized by nonfluent speech output and anomia alongside relatively preserved comprehension. The neuropathology of PNFA appears to be frontal in distribution. PNFA, due to the nonfluent speech output is rarely confused with the symptomatology of DAT. Although these two FTD syndromes are described as distinct, there are patients who demonstrate a mixed pattern with symptoms of both SD and PNFA. Lexical impairments in DAT have been studied for decades [7]. Patients with DAT have trouble recalling names and other words, often substituting pro-forms (e.g., “he,” “it”), using conceptually related words (e.g., “dog” for “horse”), or pausing when they cannot generate a target word in conversation or in structured tasks. Anomia, at least in spontaneous speech and simple picture-naming tasks, could be due to extralinguistic deficits or a deterioration of the underlying semantic/conceptual system. Extralinguistic deficits can include inattention to the task, forgetting the target word, or being distracted by related competitor responses. A semantic/conceptual impairment, defined as a loss of underlying semantic memories, would be manifested in lexical production, as well as any other task that relies on that meaning, including comprehension, knowledge of category relationships, attributes, and the like. Data from several sources can help shed light on this issue. Studies have shown that word-picture matching is relatively intact in DAT, even when naming is not, suggesting that the semantic system is sufficiently preserved to support distinguishing semantically related words from one another. Several other tasks have been used to probe the semantic system in DAT more deeply, including word definition and similarity judgments in which participants sort or arrange words so that similar items are grouped together [5]. In both definition and similarity judgment tasks, patients with DAT have performed similarly to healthy controls, giving correct (although impoverished) definitions and grouping categorically

similar words together. Semantic priming is another method to examine underlying semantic knowledge. Priming results that resemble those obtained from healthy individuals suggest that automatic semantic activation is intact in individuals with DAT However, it should be noted that priming studies of individuals with DAT have yielded contradictory results (i.e., lack of semantic priming, hyperpriming, or priming effects comparable to control participants). It has been noted that even partially degraded semantic information might result in intact semantic priming, making it difficult to ascertain the degree of semantic/conceptual loss . Sentence production in DAT is characterized by intact morphosyntactic structure (i.e., subject-verb agreement, well-formed plural and tense markings). Although sentence production in DAT is not error-free, _ demonstrated that grammatical errors made by patients with DAT are similar in type and proportion to those made by healthy elderly, suggesting that similar processes are operating in the grammar of both groups. Sentence comprehension can appear impaired in offline tasks that involve listening to and remembering instructions while selecting one of several choices in a response array or responding to information questions about the material presented The fact that patients with DAT do not show effects of syntactic complexity and that their performance correlates with measures of working memory have led authors to conclude that sentence comprehension impairments can be attributed to extralinguistic deficits in executive function (e.g., working memory). If offline sentence comprehension deficits are due to memory impairment, performance on online comprehension tasks, which minimize extralinguistic task demands, should be intact. Indeed, demonstrated in an online cross-modal naming paradigm that patients with DAT performed similarly to healthy elderly in processing subject-verb agreement. Small, Andersen, and Kempler (1997) showed that speech rate alteration can modulate sentence comprehension for patients with DAT, suggesting, again that extralinguistic factors can play a significant role in sentence processing for this population. Consistent with these data, Kavé and Levy (2003) demonstrated in both online and offline tasks that participants with DAT, like healthy controls, were sensitive to violations of tense and person. Taken together, these data suggest that grammatical processing may be grossly intact in DAT, at least with respect to relatively simple and robust grammatical phenomena (e.g., subject-verb agreement). However, the data with regard to grammatical comprehension are not altogether uniform. For instance, Price and Grossman (2005) collected data from patients with DAT using an online word detection paradigm. They found that although patients with DAT were sensitive to violations of verb transitivity, they were not sensitive to violations of thematic role assignment. Therefore, sensitive and specific tasks may reveal islands of impairment within the sphere of grammatical processing in DAT. Overall, the bulk of studies suggest that impairment in sentence comprehension is not the result of grammatical deficits per se, but rather can be attributed to extralinguistic factors, in particular, impairments in attention and working memory. Extralinguistic processing deficits have also been used to explain discourse impairments in DAT. Patients with DAT are known to have difficulty constructing an informative and coherent narrative. Their narratives are often repetitive with topic changes, unclear references (e.g., “he,” “there”), and lack of coherence and informativeness). The association between discourse and working memory in DAT was made explicit by Almor and colleagues. Almor, Kempler, MacDonald, Andersen, and Tyler (1999) demonstrated that the speech of patients with DAT contained more pronouns (compared to full nouns) than the speech of healthy participants. Furthermore, the researchers demonstrated in an online cross-modal naming paradigm that patients with DAT were less sensitive than healthy participants to the appropriateness of pronominal references in short discourses. Sensitivity to pronoun appropriateness positively correlated to working memory

scores, providing further evidence for the contribution of extralinguistic deficits to the discourse impairment observed in DAT. Extralinguistic processing deficits have also been used to explain discourse impairments in DAT. Patients with DAT are known to have difficulty constructing an informative and coherent narrative. Their narratives are often repetitive with topic changes, unclear references (e.g., "he," "there"), and lack of coherence and informativeness . The association between discourse and working memory in DAT was made explicit by Almor and colleagues. they demonstrated that the speech of patients with DAT contained more pronouns (compared to full nouns) than the speech of healthy participants. Furthermore, the researchers demonstrated in an online cross-modal naming paradigm that patients with DAT were less sensitive than healthy participants to the appropriateness of pronominal references in short discourses. Sensitivity to pronoun appropriateness positively correlated to working memory scores, providing further evidence for the contribution of extralinguistic deficits to the discourse impairment observed in DAT. In SD, word retrieval deficits are usually accompanied by word comprehension impairments, although the naming deficit is generally more severe than the comprehension deficit [6]. Additionally, patients with SD present deficits in various tasks that rely on underlying semantic/conceptual representations, including defining words sorting objects and demonstrating the use of objects [7]. Rogers et al. recently reported results of verbal and nonverbal semantic/conceptual tasks from 42 patients with SD. The patients with SD, in addition to being predictably impaired on a naming task, were also impaired on comprehension tasks using words (e.g., word-picture matching and the word version of the Palm Trees and Pyramids Test) and a semantic conceptual task with pictures (the picture version of the Palm Trees and Pyramids Test). In this and other studies, the naming deficit in SD appears to emerge early in the course of the disease and correlate significantly with performance on other semantic/conceptual tasks [7]. Data suggest that the underlying semantic/conceptual deficit in SD, like DAT, progresses. Early in the course of SD, fine distinctions are first lost between items that share many perceptual and conceptual features (e.g., "apple" and "pear"), leading to naming errors at coordinate level. Distinctions between dissimilar objects remain clearer, preserving the ability to select, for instance, the odd-man out from an array, as in the Palm Trees and Pyramids Test. At this early stage in the dementia, sufficient semantic information remains in the system to allow accurate performance on tasks of attribute and category structure (e.g., "Is pear a fruit?") and many comprehension tasks. As damage to the system progresses, more general distinctions are lost (animate vs. inanimate, abstract vs. concrete, category knowledge), interfering with an increasing number of semantically based tasks. recently documented in a 4-year longitudinal study of a patient with SD this pattern of (1) an early and persistent semantic impairment in word generation and (2) a progression of impairment on a task of implicit attribute (concrete/abstract) identification. Taken as a whole, the data suggest that the lexical deficit in SD seems to progress from one predominated by anomia to one in which an underlying semantic deficit is undeniable .Unlike DAT, the deterioration of an underlying semantic/conceptual system appears earlier and across a variety semantic/conceptual tasks. It should be mentioned that there are data that suggest the semantic/conceptual deficit in SD may not be as pervasive or as general as just stated. Several authors have proposed that visual feature information is disproportionately affected in SD. This would explain patients' inability to make judgments with regard to categories that crucially rely on perceptual information (e.g., fruits and vegetables) and their relatively preserved abilities to do so with categories that rely less on perceptual distinctions [10].

Conclusions

over the last decade. Indeed, SD appears to be one of the more straightforward frontotemporal dementia subtypes. It has a clear clinical course, which begins with language features and, with progression, affects behaviour and social cognition; this reflects early and relatively circumscribed neurodegeneration of the anterior temporal pole, which encroaches into medial prefrontal and posterior temporal regions as well as into the contralateral hemisphere with disease progression. Pathologically, it is most commonly associated with TDP43 type C and genetic causes are rare. The data reviewed here suggest that many language impairments seen in dementia are due to extralinguistic rather than linguistic deficits. Problems with memory and attention disrupt word finding in early and moderate in DAT; decreases in executive function and memory cause sentence-level processing problems seen in all three dementia syndromes. In contrast with these examples of the close connection between linguistic and non-linguistic neuropsychological functions, deficits in the semantic/conceptual system itself are predominantly responsible for the naming and word comprehension impairments in SD and in later-stage DAT. The close relationship among executive function, language abilities, and bilingualism supports the concept that cognitive reserve can delay the onset of dementia. Although the concept of cognitive reserve and preliminary data are intriguing, they raise many questions. For instance, does cognitive reserve simply refer to higher levels of skill development or to the development of additional and unique cognitive abilities, possibly metacognitive skills? Furthermore, it is unclear how cognitive reserve is acquired and the role of such factors as genetic predispositions, formal education, sociolinguistic environment, and so forth.

References

1.Abu-Akel A. A neurobiological mapping of theory of mind. Brain Res Rev. 2003;43:29–40.

2.Adenzato M, Cavallo M, Enrici I. Theory of mind ability in the behavioural variant of frontotemporal dementia: an analysis of the neural, cognitive, and social levels. Neuropsychologia. 2010;48:2–12.

3.Adolphs R. Recognizing emotion from facial expressions: psychological and neurological mechanisms. Behav Cogn Neurosci Rev. 2002;1:21–62.
4.Adolphs R, Baron-Cohen S, Tranel D. Impaired recognition of social emotions following amygdala damage. J Cogn Neurosci. 2002;14:1264–1274.
5.Anderson AK, Spencer DD, Fulbright RK, Phelps EA. Contribution of the anteromedial temporal lobes to the evaluation of facial emotion. Neuropsychology. 2000;14:526–536.
6.Baron-Cohen S, Goodhart F. The “seeing leads to knowing” deficit in autism: the Pratt and Bryant probe. Brit J Dev Psychol. 1994;12:397–402

7.Baron-Cohen S, O'Riordan M, Stone V, Jones R, Plaisted K. Recognition of faux pas by normally developing children and children with Asperger syndrome or high-functioning autism. J Autism Dev Disord. 1999;29:407–418
8.Hodges JR, Patterson K. Semantic dementia: a unique clinicopathological syndrome. Lancet Neurol. 2007;6:1004–1014.
9.Izard CE. Innate and universal facial expressions: evidence from developmental and cross-cultural research. Psychol Bull. 1994;115:288–299.
10.Kipps CM, Hodges JR. Theory of mind in frontotemporal dementia. Soc Neurosci. 2006;1:235–244.

11.Olson IR, Plotzker A, Ezzyat Y. The enigmatic temporal pole: a review of findings on social and emotional processing. Brain. 2007;130:1718–1731.